```
=> d his

     (FILE 'HOME' ENTERED AT 10:04:03 ON 29 AUG 2003)

     FILE 'USPATFULL' ENTERED AT 10:04:12 ON 29 AUG 2003
L1             2 S 112676-85-4/RN
L2             0 S 11267666-86-5/RN
L3             2 S 112676-86-5/RN
L4             2 S L1 OR L3
L5             2 S L4 AND (BENZAMIDE)
L6             2 S L4 AND ((BENZAMIDE) (P) PYRIMIDINYL)
L7             2 S L4 AND ((BENZAMIDE) (P) PYRIMIDINYL (P) PRIDINYL)
L8             2 S L7 AND (BENZAMIDE (P) METHYL (P) PYRIDINYL (P) PYRIMIDINYL (P
L9             0 S L7 AND (BENZAMIDE (W) METHYL (W) PYRIDINYL (W) PYRIMIDINYL (W
```

L4 ANSWER 3 OF 46 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:137625 CAPLUS
DN 128:281507
TI Microvascular endothelial activation in the skeletal muscles of patients with multiple organ failure
AU Helliwell, Timothy R.; Wilkinson, Ann; Griffiths, Richard D.; Palmer, T. E. Alan; McClelland, Peter; Bone, J. Michael
CS Daulby Street, Duncan Building, Department of Pathology, University of Liverpool, Liverpool, L69 3GA, UK
SO Journal of the Neurological Sciences (**1998**), 154(1), 26-34
CODEN: JNSCAG; ISSN: 0022-510X
PB Elsevier Science B.V.
DT Journal
LA English
CC 14-15 (Mammalian Pathological Biochemistry)
AB The relationship between microvascular damage and the presence of muscle fiber atrophy and necrosis has been investigated in skeletal muscle biopsies taken from 57 patients with multiple **organ failure**. Immunohistochem. studies showed no loss of capillaries and no luminal **thrombosis**, while neutrophil leukocytes were more prevalent in the patients' biopsies than in controls. Deposition of the complement membrane attack complex (C5-9MAC) in capillaries was obsd. in 41 of cases. Endothelial activation was suggested by an increased intensity of expression of ICAM-1, and by an increased proportion of capillaries expressing P selectin and E selectin, although this was not directly assocd. with neutrophil accumulation. Endothelial swelling was present in many biopsies with 38 of the biopsies having larger capillary profiles on immunohistochem. labeling for von Willebrand factor (vWF), thrombomodulin and CD34, and on Ulex europaeus agglutinin 1 binding. Endothelial swelling was confirmed by image anal. and morphometric evaluation of capillary ultrastructure, however, the capillary luminal area was not reduced as the capillaries were dilated. Increased vWF labeling was assocd. with C5-9MAC deposition and with fiber necrosis, but the vascular changes were not related to fiber atrophy nor to clin. indexes of the severity of the patients' illness. The results suggest that microvascular damage and ischemia may not be major factors in the pathogenesis of muscle fiber damage in multiple **organ failure**, but that endothelial activation is a common occurrence. The variability in the patterns of markers of endothelial activation, and the small proportion of capillaries affected, may reflect the complexity of the endothelial response to circulating or locally produced cytokines.
ST multiple organ failure muscle atrophy biochem
IT Selectins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(E-; microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
IT Cell adhesion molecules
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(ICAM-1 (intercellular adhesion mol. 1); microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
IT Selectins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(P-; microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
IT Muscle, disease
(atrophy; microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
IT Blood vessel, disease
(endothelium, injury; microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)

IT Multiple organ failure
Multiple organ failure
(microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
IT CD34 (antigen)
Thrombomodulin
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
IT Blood vessel
Blood vessel
(microvessel, endothelium; microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
IT Muscle, disease
Muscle, disease
(necrosis; microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
IT 82986-89-8, Complement C5b9 109319-16-6
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(microvascular endothelial activation in skeletal muscles of humans with multiple organ failure)
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Beutler, B; Crit Care Med 1993, V21, PS423 MEDLINE
(2) Blann, A; Br J Biomed Sci 1993, V50, P125 MEDLINE
(3) Bone, R; Crit Care Med 1992, V20, P891 MEDLINE
(4) Chad, D; Ann Neurol 1994, V35, P257 MEDLINE
(5) Clark, I; Am J Pathol 1987, V129, P192 CAPLUS
(6) Coakley, J; Br Med J 1990, P301
(7) Cybulsky, M; Lab Invest 1988, V58, P365 CAPLUS
(8) Dahlback, L; Acta Chir Scand 1966, V131, P430 MEDLINE
(9) de Bleeker, J; J Neuropathol Exp Neurol 1994, V53, P369
(10) Dubowitz, V; Muscle Biopsy:A Practical Approach 1989
(11) Dustin, M; Nature 1989, V341, P619 CAPLUS
(12) Emslie-Smith, A; Ann Neurol 1990, V27, P343 MEDLINE
(13) Fries, J; Am J Pathol 1993, V143, P725 CAPLUS
(14) Gattinoni, L; New Engl J Med 1995, V333, P1025 CAPLUS
(15) Ghadially, F; Ultrastructural Pathology of the Cell and Matrix:A Text and Atlas of Physiological and Pathological Alterations in the Fine Structure of Cellular and Extracellular Components 1982, P776
(16) Harrison, D; Adv Exp Biol Med 1988, V222, P623 MEDLINE
(17) Hattori, R; J Biol Chem 1989, V264, P9053 CAPLUS
(18) Helliwell, T; J Pathol 1991, V164, P307 MEDLINE
(19) Helliwell, T; Neuropathol Appl Neurobiol 1987, V13, P297 MEDLINE
(20) Kahaleh, M; Clin Exp Rheumatol 1990, V8, P595 MEDLINE
(21) Kuzu, I; J Clin Pathol 1992, V45, P143 MEDLINE
(22) Mastaglia, F; Skeletal Muscle Pathology 1992, P718
(23) McLaughlin, P; Anticancer Res 1992, V12, P1243 CAPLUS
(24) Munro, J; Am J Pathol 1989, V135, P121 CAPLUS
(25) Newman, W; J Clin Immunol 1993, V150, P644 CAPLUS
(26) Pober, J; Lab Invest 1991, V64, P301 MEDLINE
(27) Redl, H; Am J Pathol 1991, V139, P461 MEDLINE
(28) Renard, N; J Pathol 1995, V176, P279 CAPLUS
(29) Schumaker, P; Int Care Med 1987, V13, P223
(30) Smith, C; J Clin Invest 1989, V83, P2008 CAPLUS
(31) van Deventer, S; Blood 1990, V76, P2520 CAPLUS

=>

L4 ANSWER 11 OF 46 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AN 1999423977 EMBASE
TI [Pathophysiology and diagnosis of coagulation activation in sepsis].
PATHOPHYSIOLOGIE UND DIAGNOSTIK DER GERINNUNGSAKTIVIERUNG BEI SEPSIS.
AU Ostermann H.; Bohrer H.
CS Dr. H. Ostermann, Medizinische Klinik/Poliklinik III, Ludwig-Maximilians-Univ. Munchen, Marchioninistrasse 15, D-81377 Munchen, Germany
SO Anasthesiologie und Intensivmedizin, (**1999**) 40/11 (796-799).
Refs: 32
ISSN: 0170-5334 CODEN: ANIMD2
CY Germany
DT Journal; Article
FS 024 Anesthesiology
025 Hematology
LA German
SL English; German
AB Sepsis can be regarded as a systemic inflammatory reaction often accompanied by disseminated intravascular coagulation (DIC) which is supposed to be initiated by the expression of tissue factor for example by activated monocytes and endothelial cells. The hallmark of DIC is the intravascular generation of thrombin which leads to fibrin formation. Diagnosis of DIC is likely if sepsis is accompanied by the occurrence of intravascular soluble fibrin, a decrease in coagulation inhibitors (antithrombin) and thrombocytopenia. The most sensitive and specific test for DIC seems to be the detection of fibrin monomers. Clinical symptoms of DIC are caused simultaneously by consumption of coagulation factors (bleeding) and intravascular **thrombosis** (**organ failure**).
CT Medical Descriptors:
*sepsis
*disseminated intravascular clotting
blood clotting
monocyte
endothelium cell
fibrin formation
disease association
human
article

L4 ANSWER 12 OF 46 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AN 1999362498 EMBASE
TI Coagulation and fibrinolysis in patients undergoing operation for ruptured and nonruptured infrarenal abdominal aortic aneurysms.
AU Adam D.J.; Ludlam C.A.; Ruckley C.V.; Bradbury A.W.
CS D.J. Adam, Vascular Surgery Unit, Univ. Dept. of Clinic./Surg. Sci., Royal Infirmary, Edinburgh EH3 9YW, United Kingdom
SO Journal of Vascular Surgery, (**1999**) 30/4 (641-650).
Refs: 31
ISSN: 0741-5214 CODEN: JVSUES
CY United States
DT Journal; Article
FS 009 Surgery
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LA English
SL English
AB Purpose: Hemorrhage and **thrombosis** predisposing to myocardial infarction, multiple **organ failure**, and thromboembolism account for the majority of the morbidity and mortality associated with repair of ruptured and nonruptured abdominal aortic aneurysms (AAAs). The aim of this study was to examine coagulation and fibrinolysis in patients operated on for ruptured and nonruptured infrarenal AAAs. Methods. Ten patients operated on for ruptured and 9 patients operated on for nonruptured AAAs were studied. Tissue plasminogen activator (t-PA) antigen, thrombinantithrombin (TAT), and D-dimer were measured before induction of anesthesia. Plasminogen activator inhibitor (PAI) activity, t-PA activity, and prothrombin fragment (PF) 1+2 were measured before induction of anesthesia, immediately before aortic clamp release, and 5 minutes and 24 hours after aortic clamp release. Results: Preoperatively, ruptured AAA was associated with significantly elevated t-PA antigen (median 15.7 ng/mL, range 9.0 to 22.1 ng/mL versus nonrupture: median 6.6 ng/mL, range 4.7 to 16.4 ng/mL; P < .01, Mann-Whitney test), increased PAI activity (median 36.5 arbitrary units/mL, range 20.6 to 38.8 arbitrary units/mL versus nonrupture: median 8.2 arbitrary units/mL, range 3.2 to 21.7 arbitrary units/mL; P < .001), reduced t-PA activity (median 0.12 IU/mL, range 0.06 to 0.4 IU/mL versus nonrupture: median 0.49 IU/mL, range 0.14 to 3.2 IU/mL; P < .01), elevated TAT (median 135.5 .mu.g,/L, range 61.2 to 209.4 .mu.g/L versus nonrupture: median 21.6 .mu.g/L, range 6.6 to 180.4 .mu.g/L; P < .02) and elevated PF 1+2 (median 9.0 nmol/L, range 5.4 to 11.6 nmol/L versus nonrupture: median 2.2 nmol/L, range 0.7 to 7.1 nmol/L, P < .001). There was no significant difference in preoperative D-dimer levels (median 3460 ng/mL, range 1236 to 7860 ng/mL versus nonrupture: median 1642 ng/mL, range 728 to 5334 ng/mL; P = .07). The differences in PAI activity, t-PA activity, and PF 1+2 persisted throughout the course of surgery, but there was no significant difference between the groups at 24 hours. Conclusion: These novel data demonstrate that ruptured AAA repair is associated with inhibition of systemic fibrinolysis and intense thrombin generation. Similar changes are seen in nonruptured AAA but are of a lesser magnitude. This procoagulant state may contribute to the microvascular and macrovascular **thrombosis** that leads to myocardial infarction, multiple **organ failure**, and thromboembolism.
CT Medical Descriptors:
*abdominal aorta aneurysm: SU, surgery
*aneurysm rupture: SU, surgery
*thromboembolism: CO, complication
*thromboembolism: DT, drug therapy
*thromboembolism: PC, prevention
*heart infarction: CO, complication
*heart infarction: DT, drug therapy
*heart infarction: PC, prevention
multiple organ failure: CO, complication

multiple organ failure: DT, drug therapy
multiple organ failure: PC, prevention
aneurysm surgery
thrombosis prevention
anticoagulant therapy
heparinization
human
male
female
clinical article
aged
article
priority journal
Drug Descriptors:
*heparin: DT, drug therapy
tissue plasminogen activator
RN (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (tissue plasminogen activator) 105913-11-9

=>

```
=> s wo2001012621/pn
L1             1 WO2001012621/PN
                 (WO2001012621/PN)

=> d l1 fam

L1    ANSWER 1 OF 1  INPADOC  COPYRIGHT 2003 EPO on STN

PATENT FAMILY INFORMATION
 AN   145684263 INPADOC
```

PRAI			AI		
US 1999-148795P	P	19990812	AU 2000-69096	A	20000811
			BR 2000-13551	A	20000811
			CA 2000-2381882	A	20000811
			CN 2000-814178	A	20000811
			CZ 2002-534	A	20000811
			EP 2000-957485	A	20000811
			HU 2003-340	A	20000811
			NO 2002-713	A	20020212
			SK 2002-357	A	20000811
			WO 2000-US22445	A	20000811
US 1999-166922P	P	19991122	AU 2000-69096	A	20000811
			BR 2000-13551	A	20000811
			CA 2000-2381882	A	20000811
			CN 2000-814178	A	20000811
			CZ 2002-534	A	20000811
			EP 2000-957485	A	20000811
			HU 2003-340	A	20000811
			NO 2002-713	A	20020212
			SK 2002-357	A	20000811
			WO 2000-US22445	A	20000811
US 2000-211517P	P	20000614	AU 2000-69096	A	20000811
			BR 2000-13551	A	20000811
			CA 2000-2381882	A	20000811
			CN 2000-814178	A	20000811
			CZ 2002-534	A	20000811
			EP 2000-957485	A	20000811
			HU 2003-340	A	20000811
			NO 2002-713	A	20020212
			SK 2002-357	A	20000811
			WO 2000-US22445	A	20000811
WO 2000-US22445	W	20000811	AU 2000-69096	A	20000811
			BR 2000-13551	A	20000811
			CA 2000-2381882	A	20000811
			EP 2000-957485	A	20000811
			HU 2003-340	A	20000811
			NO 2002-713	A	20020212
			SK 2002-357	A	20000811

AI			PI		
AU 2000-69096	A	20000811	AU 2000069096	A5	20010313
BR 2000-13551	A	20000811	BR 2000013551	A	20030617
CA 2000-2381882	A	20000811	CA 2381882	AA	20010222
CN 2000-814178	A	20000811	CN 1378541	T	20021106
CZ 2002-534	A	20000811	CZ 2002000534	A3	20020717
EP 2000-957485	A	20000811	EP 1218369	A1	20020703
HU 2003-340	A	20000811	HU 2003000340	AB	20030628
NO 2002-713	A	20020212	NO 2002000713	A	20020412
			NO 2002000713	A0	20020212
SK 2002-357	A	20000811	SK 2002000357	A5	20020702
WO 2000-US22445	A	20000811	WO 2001012621	A1	20010222

4 priorities, 10 applications, 11 publications

=>